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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/797,903	03/10/2004	Yuji Yamamoto	2003946-0080 (FP04-0096-0	3373

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CHOATE, HALL & STEWART LLP
TWO INTERNATIONAL PLACE
BOSTON, MA 02110

EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	**PAPER NUMBER**
1614	

NOTIFICATION DATE	DELIVERY MODE
07/23/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@choate.com

Office Action Summary	Application No.	Applicant(s)	
	10/797,903	YAMAMOTO ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/4/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12 and 14-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12, 14-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/4/2008, 1 sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 4/4/2008 has been received and entered into the present application.

Claims 12, 14-20 are currently pending. Accordingly, claims 1-11 and 13 have been cancelled, claims 12, 14-17 have been amended.

As reflected by the attached, completed copy form PTO/SB/08A (one page total), the Examiner has considered the cited reference.

Applicant's arguments, filed 4/4/2008 have been fully considered. Rejections not reiterated from the previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Withdrawal of Newly Added Hydrate Specie: Election by Original Presentation

Applicant's amendment to add a hydrate specie in claims 12, 14-15, 17-20 have been carefully considered in light of the subject matter that was elected and examined in the previous non-final Office Action.

The MPEP states at 819:

"The general policy of the Office is not to permit the Applicant to shift to claiming another invention after an election is once made and action given to the elected subject matter."

Newly amended claims 12, 14-17 are directed to a patentably distinct specie of the invention originally claimed for the following reasons: originally filed claims 12, 14-17 were directed to a single agent therapy comprising the elected compound for the treatment of cancer, whereas the newly amended claims are not directed to the elected species but hydrates of the specie thereof. Accordingly, the subject matter of newly amended claims 12, 14-17 is a patentably distinct species of the invention that was both originally claimed and examined.

Since Applicant has received an action on the merits for the originally presented invention directed to the administration of the elected compound for the treatment of cancer, this invention has been constructively elected by original presentation for prosecution on the merits. As a result, the amendment and inclusion of a hydrate is withdrawn from consideration as being directed to a non-elected invention. Please see 37 CFR 1.142(b) and MPEP 821.03. As stated in the MPEP at 818.02(a), "The claims originally presented and acted upon by the Office on the merits determine the invention elected by an Applicant in the application, and in any request for continued examination (RCE) which has been filed for the application. Subsequently presented claims to an invention other than that acted upon should be treated as provided in MPEP 821.03."

For these reasons, the inclusion of a hydrate specie of the elected compound is withdrawn from consideration pursuant to 37 CFR 1.142(b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner

to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12 and 14 are rejected under 35 U.S.C. 102(b) as being unpatentable over Funahasi et al (WO 02/032872, cited by Applicant).

Examiner is using the Japanese WO 02/032871 document for its publication date and is providing US Patent 7, 253, 286 as an English language equivalent of that document.

Funahasi et al. disclose the elected compound: claim 1 discloses R_1 and R_2 as hydrogen (claim 1), R^{a12} is the cyano taught by the formula in column 904, line 40, second compound, (claim 1), Y^{a1} is represented by the formula in column 903, line 35, first compound, where W^{31} and W^{32} are each independently an optionally substituted carbon atom (claim 1) and Z^{12} is an alicyclic hydrocarbon group (claim 1). This particular combination teaches the compound elected by Applicant. Additionally, Funahasi et al. describes utility of the elected compound having angiogenesis inhibitory action (column 2, lines 63-67) and tumor cell proliferation (column 83, last line) inhibitory action in treatment of diseases including as a "pulmonary treatment agent" (column 34, line 22), a powerful angiogenesis-inhibiting and cancer cells growth inhibiting effect (column 1, last paragraph) and useful for amelioration, prevention and treatment of various diseases associated with abnormal increase in angiogenesis (column 2, first paragraph). With respect, to the election of small cell lung cancer, given that the treatment of cancer and angiogenesis is taught by Funahasi et al. one of ordinary skill in the art would have a reasonable expectation of success that the elected compound could in fact be an effective treatment for small cell lung cancer.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a)

Claims 12, 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Funahasi et al. (WO 02/032872, cited by Applicant) in view of Hibi et al. (reference provided by Applicant).

Examiner is using the Japanese WO 02/032871 document for its publication date and is providing US Patent 7, 253, 286 as an English language equivalent of that document.

Funahasi et al. disclose the elected compound: claim 1 discloses R_1 and R_2 as hydrogen (claim 1), R^{a12} is the cyano taught by the formula in column 904, line 40, second compound, (claim 1), Y^{a1} is represented by the formula in column 903, line 35, first compound, where W^{31} and W^{32} are each independently an optionally substituted carbon atom (claim 1) and Z^{12} is an alicyclic hydrocarbon group (claim 1). This particular combination teaches the compound elected by Applicant. Additionally, Funahasi et al. describes utility of the elected compound having angiogenesis inhibitory action (column 2,

lines 63-67) and tumor cell proliferation (column 83, last line) inhibitory action in treatment of diseases including as a "pulmonary treatment agent" (column 34, line 22).

Hibi et al. discloses that lung cancer cells have been known to produce autocrine growth factors which include gastrin-releasing peptide, leading the author to study c-kit expression in small cell lung cancer (page 2295, left column, paragraph 2). The researchers conclude that c-Kit expression is present in small cell lung cancer.

One of ordinary skill in the art at the time of the invention would have found it prima facie obvious to employ the results found in Hibi et al. with a reasonable expectation of success because of the clear antiproliferative activity of the elected compound (Funahasi et al.) in a variety of tumor cell lines including the elected small cell lung cancer. Motivation to do so flows logically since Hibi et al. teaches that c-Kit expression is found in small cell lung cancer and Funahasi et al. teach the elected compound as an effective treatment for pulmonary treatment.

The explanation of an effect obtained when using a compound cannot confer novelty on a known process if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. In other words, even if the inhibition of c-Kit kinase was not itself recognized as a pharmacological effect of administering the elected compound of Funahasi et al. to a patient exhibiting proliferation of cancer cells such as small cell lung cancer, such an effect (treatment of pulmonary conditions including tumors) is already known in the prior art. Though new properties of a compound are not doubt important contributions to scientific and pharmaceutical development, the assessment of patentability under 35 U.S.C. 103 is based upon the therapeutic applications and effects of the compounds, not the mechanisms or properties by which they exert such a therapeutic effect.

Please also see Ex Parte Novitski, 26 USPQ2d 1389 (Bd. Pat. App. And Inter. 1993), which stated, "The Board rejected a claim directed to a method for protecting a plant from plant pathogenic nematodes by inoculating the plant with a nematode inhibiting strain of P. cepacia. A U.S. Patent to Dart

disclosed inoculating using P.cepacia type Wisconsin 526 bacteria for protecting the plant from fungal disease. Dart was silent as to nematode inhibition but the Board concluded that nematode inhibition was an inherent property of the bacteria. The Board noted that Applicant had stated in the specification that Wisconsin 526 an 18 percent nematode inhibition rating." Analogously, in the present case, though Funahasi does not explicitly note the function of the elected compound as a c-Kit kinase inhibitor, such a property, though only now recognized by Applicant, is an inherent property of the elected compound, absent factual evidence to the contrary.

Applicant's Response

Applicant contends that the Examiners argument is flawed since it relies on an erroneous logical assumption. Further, Applicant argues that if c-Kit expression in small cell lung cancer is the source of motivation for using the elected compound to treat small cell lung cancer, then there must also be some express teaching in the prior art that the elected compound inhibits c-Kit kinase. Finally, Applicant argues that the Examiner cannot presume that because c-Kit is expressed in small cell lung cancer and because the elected compound is taught as a "pulmonary treatment agent" in Funahasi et al. then it must be acting as a c-Kit kinase inhibitor in Funahasi et al.

Response to Applicant's Arguments

Examiner contends that Applicant has misinterpreted the rejection mailed on 12/11/2007. In fact, Examiner contends that a compound cannot confer novelty on a known process if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. In other words, even if the inhibition of c-Kit kinase was not itself recognized as a pharmacological effect of administering the elected compound of Funahasi et al. to a patient exhibiting proliferation of cancer cells such as small cell lung cancer, such an effect (treatment of pulmonary conditions including tumors) is already known in the prior art.

Examiner supplements the rejection with Hibi et al. to demonstrate that if the elected compound in fact demonstrates c-Kit kinase activity or inhibition, one of ordinary skill in the art would have a reasonable expectation that the elected compound would treat small cell lung cancer since per Hibi et al. c-Kit is overexpressed in small cell lung cancer tumors.

Conclusion

No claims are found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614